Amendments to the Specification

Please replace the paragraph beginning at page 3, line 14, with the following redlined paragraph.

Figure 3 depicts the comparison of the predicted amino acid sequences of the BVH-P7 open reading frames from Spy74, Spy70, Spy69, Spy68, Spy 60, ATCC12357, ATCC700294 S. pyogenes strains by using the program Clustal W from ~~MacVector~~MACVECTOR® ~~-~~sequence analysis software (version 6.5). Underneath the alignment, there is a consensus line where * and . characters indicate identical and similar amino acid residues, respectively.

Please replace the paragraph beginning at page 15, line 10, with the following redlined paragraph.

According to another aspect, there are provided pharmaceutical compositions comprising one or more Streptococcal polypeptides of the invention in a mixture with a pharmaceutically acceptable adjuvant. Suitable adjuvants include (1) oil-in-water emulsion formulations such as ~~MF59™~~ MF59®, SAF™, Ribi™; (2) Freund's complete or incomplete adjuvant; (3) salts, *e.g.,* ~~i.e.~~ $AlK(SO_4)_2$, $AlNa(SO_4)_2$, $AlNH_4(SO_4)_2$, $Al(OH)_3$, $AlPO_4$, silica, kaolin; (4) saponin derivatives such as ~~Stimulon™~~STIMULON® or particles generated therefrom such as ISCOMs (immunostimulating complexes); (5) cytokines such as interleukins, interferons, macrophage colony stimulating factor (M-CSF), tumor necrosis factor (TNF); (6) other substances such as carbon polynucleotides, *e.g.,* ~~i.e.~~ poly IC and poly AU, detoxified cholera toxin (CTB) and E. coli heat labile toxin for induction of mucosal immunity. A more detailed description of adjuvant is available in a review by M. Z. I Khan et al. in Pharmaceutical Research, vol. 11, No. 1 (1994) pp2-11, and also in another review by Gupta et al., in Vaccine, Vol. 13, No. 14, pp1263-1276 (1995) and in WO 99/24578, which are herein incorporated by reference. Preferred adjuvants include QuilA™ (an adjuvant containing saponins from the bark of *Quillaja saponaria*), QS21™ (purified fraction of Saponin extracted from *Quillaja saponaria*), ~~Alhydrogel™~~ALHYDROGEL® (an aluminum hydroxide (hydrated alumina) adjuvant), and Adjuphos™ (an aluminum phosphate adjuvant).

Please replace the paragraph beginning at page 17, line 27, with the following redlined paragraph.

Suitable stringent conditions for ~~hybridation~~ hybridization can be readily determined by one of skilled in the art (see for example Sambrook et al., (1989) Molecular cloning : A Laboratory Manual, 2nd ed, Cold Spring Harbor, N.Y.; Current Protocols in Molecular Biology, (1999) Edited by Ausubel F. M. et al., John Wiley & Sons, Inc., N.Y.).

Please replace the paragraph beginning at page 24, line 29, with the following redlined paragraph.

The coding region of S. pyogenes BVH-P7 (SEQ ID NO: 1) gene was amplified by PCR (~~Robocycler~~ROBOCYCLER® Gradient 96 Temperature cycler, ~~Stratagene~~STRATAGENE®, LaJolla, CA) from genomic DNA of serotype M1 S. pyogenes strain ATCC700294 using the following ~~oligonucleotide~~ oligonucleotide primers that contained base extensions for the addition of restriction sites *Nde*I (CATATG) and *Not*I (GCGGCCGC): DMAR293 and DMAR294, which are presented in Table 1. PCR products were purified from agarose gel using a QIA®quick gel extraction kit from QIAGEN®~~QIAgen~~ following the manufacturer's instructions (Chatsworth, CA), and digested with *Nde*I and *Not*I (Amersham Pharmacia Biotech Inc, Baie d'Urfé, Canada). The pET-21b(+) vector (NOVAGEN®~~Novagen~~, Madison, WI) was digested with *Nde*I and *Not*I and purified from agarose gel using a QIA®quick gel extraction kit from ~~QIAgen~~ QIAGEN® (Chatsworth, CA) The *Nde*I-*Not*I PCR products were ligated to the *Nde*I-*Not*I pET-21b(+) expression vector. The ligated products were transformed into E. coli strain DH5• [ϕ80d*lac*ZΔM15 Δ(*lac*ZYA-*arg*F)U169 *end*A1 *rec*A1 *hsd*R17(r_K-m_K+) *deo*R *thi*-1 *sup*E44 λ*gyr*A96 *rel*A1] (Gibco BRL, Gaithersburg, MD) according to the method of Simanis (Hanahan, D. DNA Cloning, 1985, D. M. Glover (ed), pp. 109-135). Recombinant pET-21b(+) plasmid (rpET21b(+)) containing BVH-P7 gene was purified using a QIAGEN®~~QIAgen~~ plasmid kit (Chatsworth, CA) and DNA insert was sequenced (Taq Dye Deoxy Terminator Cycle Sequencing kit, ABI, Foster City, CA).

Please replace the paragraph beginning at page 28, line 9, with the following redlined paragraph.

The coding regions of BVH-P7 (SEQ ID NO: 1) gene without its leader peptide region was amplified by PCR (ROBOCYCLER®~~Robocycler~~ Gradient 96 Temperature cycler, STRATAGENE®~~Stratagene~~, Lajolla, CA) from genomic DNA of serotype M1 S. pyogenes strain ATCC700294 using oligonucleotide primers DMAR480a and DMAR481a that contained base extensions for the addition of restriction sites *Bam*HI (GGATCC) and *Sal*I (GTCGAC) which are described in Table 1. The PCR products were purified from agarose gel using a QIA®quick gel extraction kit from QIAGEN® ~~QIAgen~~ (Chatsworth, CA), digested with restriction enzymes (Amersham Pharmacia Biotech Inc, Baie d'Urfé, Canada). The pCMV-GH vector (Laboratory of Dr. Stephen A. Johnston, Department of Biochemistry, The University of Texas, Dallas, Texas) was digested with *Bam*HI and *Sal*I and purified from agarose gel using the QIA®quick gel extraction kit from QIAGEN® ~~QIAgen~~ (Chatsworth, CA). The *Bam*HI-*Sal*I DNA fragment was ligated to the *Bam*HI-*Sal*I-pCMV-GH vector to create the hGH-BVH-P7 fusion protein under the control of the CMV promoter. The ligated product was transformed into E. coli strain DH5• [ϕ80d*lac*ZΔM15 Δ(*lac*ZYA-*arg*F)U169 *end*A1 *rec*A1 *hsd*R17(r_K-m_K+) *deo*R *thi*-1 *sup*E44 λ$^-$ *gyr*A96 *rel*A1] (Gibco BRL, Gaithersburg, MD) according to the method of Simanis (Hanahan, D. DNA Cloning, 1985, D. M. Glover (ed), pp. 109-135). The recombinant pCMV plasmid was purified using a QIAGEN®~~QIAgen~~ plasmid kit (Chatsworth, CA) and the nucleotide sequence of the DNA insert was verified by DNA sequencing.

Please replace the paragraph beginning at page 29, line 23, with the following redlined paragraph.

The recombinant pET-21b(+) plasmid with BVH-P7 (SEQ ID NO: 1) gene was used to transform by electroporation (Gene Pulser II apparatus, BIO-RAD® Labs, Mississauga, Canada) E. coli strain Tuner (DE3) (F$^-$ompT hsdS_B ($r^-_B m^-_B$) gal dcm lacYI (DE3)) (~~Novagen~~NOVAGEN®, Madison, WI). In this strain of E. coli, the T7 promotor controlling expression of the recombinant protein is specifically recognized by the T7 RNA polymerase (present on the λDE3 prophage) whose gene is under the control of the lac promotor which is inducible by isopropyl-β-d-thio-galactopyranoside (IPTG). The transformants Tuner (DE3)/rpET21 (+) were grown at 37° C with agitation at 250 rpm in LB broth (peptone 10 g/L, yeast extract 5 g/L, NaCl 10 g/L) containing 100 μg of carbenicillin (Sigma-Aldrich Canada

Ltd., Oakville, Canada) per ml until the A_{600} reached a value of 0.6. In order to induce the production of BVH-P7 His-tagged S. pyogenes recombinant protein, the cells were incubated for 3 additional hours in the presence of IPTG at a final concentration of 0.1 mM. Induced cells from a 500 ml culture were pelleted by centrifugation and frozen at -70° C.

Please replace the paragraph beginning at page 30, line 4, with the following redlined paragraph.

The purification of the BVH-P7 His-tagged recombinant protein from the non-soluble fraction of IPTG-induced Tuner (DE3)/rpET21b(+) was done by affinity chromatography based on the properties of the His•Tag sequence (6 consecutive histidine residues) to bind to divalent cations (Ni^{2+}) immobilized on the His•Bind metal chelation resin. Briefly, the pelleted cells obtained from a 500 mL culture induced with IPTG was resuspended in lysis buffer (20 mM Tris, 500 mM NaCl, 10 mM imidazole, pH 7.9) containing 6M Guanidine-HCl, sonicated and centrifuged at 12,000 X g for 20 min to remove debris. The supernatant was incubated with Ni-NTA agarose resin (QIAGEN®~~Qiagen~~, Mississauga, Ontario, Canada) for 45 min at 4°C. The BVH-P7 His-tagged S. pyogenes recombinant protein was eluted from the resin with a solution containing 6M Guanidine-HCl and 250 mM imidazole-500mM NaCl-20 mM Tris, pH 7.9. The removal of the salt and imidazole from the samples was done by dialysis against 10mM Tris and 0.9% NaCl, pH 7.9 overnight at 4°C. The amount of recombinant protein was estimated by MicroBCA (Pierce, Rockford, Illinois).

Please replace the paragraph beginning at page 33, line 20, after Table 4, with the following redlined paragraph.

[1] The mice S1 to S8 were injected subcutaneously three times at three-week intervals with 20 µg of purified BVH-P7 recombinant protein mixed with 10 µg of QuilA™ ~~QuilA~~ adjuvant (Cedarlane Laboratories, Hornby, Canada). The sera were diluted (1/50).

Please replace the paragraph beginning at page 34, line 20, with the following redlined paragraph.

New Zealand rabbits (Charles River laboratories, St-Constant, Canada) ~~were~~ are injected subcutaneously at multiple sites with 50 μg and 100 μg of the BVH-P7 His-tagged recombinant protein that ~~was~~ is produced and purified as described in Example 4 and adsorbed to ALHYDROGEL® ~~Alhydrogel~~ adjuvant (~~Superfos~~ SUPERFOS® Biosector a/s). Rabbits ~~were~~ are immunized three times at three-week intervals with the BVH-P7 His-tagged recombinant protein. Blood samples ~~were~~ are collected three weeks after the third injection. The antibodies present in the serum ~~were~~ are purified by precipitation using 40% saturated ammonium sulfate. Groups of 10 female CD-1 mice (Charles River) ~~were~~ are injected intravenously with 500 μl of purified serum collected from rabbits immunized with the BVH-P7 His-tagged recombinant protein, or rabbits immunized with an unrelated control recombinant protein. Eighteen hours later the mice ~~were~~ are challenged with approximately 2×10^7 CFU of the type 3 S. pyogenes strain ATCC12384. Samples of the S. pyogenes challenge inoculum ~~were~~ are plated on blood agar plates to determine the CFU and to verify the challenge dose. Deaths ~~were~~ are recorded for a period of 5 days.

Please replace the paragraph beginning at page 35, line 8, with the following redlined paragraph.

Groups of 8 female Balb/c mice (Charles River, St-Constant, Québec, Canada) were immunized subcutaneously three times at two-week intervals with 20 μg of affinity purified BVH-P7 His-tagged recombinant protein in presence of 10 μg of QuilA™ adjuvant (Cedarlane Laboratories Ltd, Hornby, Canada) or, as control, with QuilA™ adjuvant alone in PBS. Blood samples were collected from the orbital sinus on day 1, 14 and 28 prior to each immunization and two weeks (day 42) following the third injection. One week later the mice were challenged with approximately 3×10^6 CFU of the type 3 S. pyogenes strain ATCC 12384. Samples of the S. pyogenes challenge inoculum were plated on blood agar plates to determine the CFU and to verify the challenge dose. Deaths were recorded for a period of 7 days. Four of eight mice

immunized with purified recombinant BVH-P7 protein were protected against the lethal challenge, compared to only 12 % (1/8) of mice which received the adjuvant alone (Table 1).